Applications of Fluorescence-Assisted Infrared Microspectroscopy to the Study of Osteoporosis

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Osteoporosis is a disease characterized by reduction in bone mass, resulting in a fragile skeleton. It is clear that bone loss occurs in the disease; however, the quality of bone remodeled after the onset of the disease is unknown. We are using synchrotron infrared microspectroscopy to analyze the chemical composition of bone remodeled before versus after the onset of osteoporosis. In our study, female cynomolgus monkeys were ovariectomized or sham-ovariectomized. After ovariectomization, many monkeys developed osteoporosis. After surgery, the monkeys were administered fluorescent drugs every six months for two years prior to necropsy. These fluorochromes (tetracycline, calcein, and xylenol orange) are taken into newly remodeled bone tissue. Thus, by combining fluorescence microscopy and infrared microspectroscopy, we are able to identify and compare the chemical composition of new versus older bone growth. We are examining the mineral/matrix ratios, mineral composition, and matrix composition as a function of bone age.

To date, we have used fluorescence microscopy to identify regions of new bone growth after ovariectomy and examined them with the synchrotron infrared microscope. As expected, we find that these regions of new bone growth are less mineralized than mature bone. In addition, the chemical composition of bone from Intact versus Ovx monkeys has been compared. Results from overall composition distributions (labeled + non-labeled bone) reveal similar carbonate / protein and phosphate / protein ratios, but increased acid phosphate content and different collagen structure in the Ovx animals. Analysis of the fluorochrome-labeled bone indicates similar degrees of mineralization in bone remodeled after one year, but decreased mineralization in Ovx bone remodeled two years after surgery. Thus, bone from monkeys with osteoporosis can be characterized as having abnormal collagen structure and reduced rates of mineralization. Coupled with factors such as trabecular architecture and bone shape and size, these ultra structural factors may play a contributing role in the increased bone fragility in osteoporosis.